Antimicrobial Copper

An ally for Public Health

Cu

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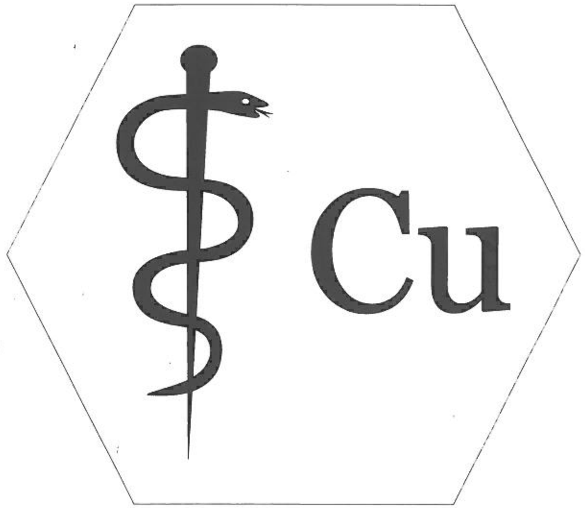

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Abstract

This study regards the use of antimicrobial copper alloys for the protection of public health, and places emphasis on the implementation of this innovative action in the health sector, especially in a hospital environment. Copper's ions mechanism actions as well as the germicidal efficacy of a wide range of Gram- and Gram+ pathogens and viruses are being analyzed. Emphasis is given to the ions' action related to the membrane depolarization and the DNA disruption. Models of germicidal efficacy are approached and analyzed theoretically based on the result. Moreover, historical paths of copper and its' applications as well as studies in universities or hospitals worldwide are mentioned. Emphasis is also placed on application of antimicrobial copper in the Intensive Care Unit areas that are characterized by increased microbial load. Finally the economic impact of this particular application at a time of economic austerity will be discussed. The overall approach to the antimicrobial copper use must not contradict the campaign of the World Health Organization «Clean Hands», which is the basis of efforts made to reduce the transmission of microbes.

Introduction

Mankind has been characterized by various development phases, one of which is the "Bronze Age". In this period, people are discovering copper as a chemical element and use it for the manufacture of various items concerning personal use as well as martial arts (1) Copper as a metal is known to be classified in Mendeleev's Periodic Table with the atomic number 29, by the chemical synthesis of monovalent or divalent. As Cuo, copper does not exist in nature but as a transition element of chemical reactions. It is also known that copper as pure metal in the form of alloys, was used in ancient times to create jewelry and items of high value.

The first reports of copper were recorded in texts of the Assyrians and Egyptians dating back early in 4000 BC (2) In one of the oldest books of Edwin Smith papyrus mentions the use of copper for sterilizing not only chest wounds but also drinking water (2600-2200p.Ch.) (3).

Hippocrates (460-480 BC) in his reports makes observations about the beneficial capabilities of copper in the treatment of wounds (4) Centuries following, are characterized by the full utilization of copper and its alloys to create weapons such as swords, shields, helmets, gaiters, etc., which are preserved until these days in an excellent condition. In the more recent centuries, copper and its alloys are used in the manufacture of cookware (provided the electrographic determination), as well as to create pipes for water supply in urban areas. As a good conductor of electricity, copper nowadays is the main material used for the wired transfer of electric current and the generating coil aiming at generating energy.

The association of copper with Health, has begun to concern the scientific community since the last century, when the first comments on the lack of deceased workers in copper mines of France during the 18th century cholera epidemic of this region, created many scientific questions without answers (3) Moreover, the use of copper containers for storing water from the River Ganges in India, which by definition was polluted due to maintenance of sacred cows, and its use by humans, found no difficulty in dysentery or contamination if it was used after 24 hours.

Over the last decade, in the United States, over 300 metal alloys containing copper over 60% have been certified by the Environmental Protection Agency and characterized as having antimicrobial activity.

Basic studies completed in the following hospitals: the Medical University of South Carolina, the Ralph H Johnson Veterans Administration Medical Center, and the Memorial Sloan Kettering Cancer Center (New York City). In the above hospitals' ICUs, antimicrobial copper efficacy was tested through the replacement of all multi-touched surfaces (bed rails, IV poles, trays etc) with others made of antimicrobial copper alloys. The microbial burden of these surfaces was estimated by samples' taking. Antimicrobial copper application demonstrated that the microbicidal activity of antimicrobial copper is over 95% in the first two hours (5). Another trial at Selly Oak Hospital of Birmingham has shown that on copper surfaces, when compared to others the contamination was reduced. Results of another clinical trial in Hospital del Cobre, in Calama (Chile) demonstrated a 90% microorganisms reduction on copper-made items.

In Germany, in the Asklepios Clinic (Hamburg) in the geriatric ward, all door handles and light switches as well as all items (multi –touched surfaces) of all bathrooms were either replaced by others made of antimicrobial copper alloys or were implemented with copper. Results of this research demonstrated a significant reduction in contamination.

In Finland, University Department of Public Health conducted a research at a nursing home, in Helsinki. In this research, all items made of antimicrobial copper alloys' contamination were compared to other items frequently used in patient rooms. The items where samples were taken were dressing trolleys, door handles, rails, handrails, shower drains and push buttons. Non-copper items showed high concentration in bacterias, such as Staphylococcus aureus, E. coli and Candida albicans. On the other hand, on copper alloy surfaces/items, Gram-positive bacilli and cocci were found.

One of the important applications was in an isolation unit of TOKUDA hospital in Sofia, Bulgaria, with full implementation of antimicrobial copper, in all objects and the contact surfaces. These multi – touched surfaces were those of trolleys, bed rails, IV pole hand rails (6) (Fig. 1). We would say, after the above, that mankind will enter a new era, the "era of antimicrobial copper."

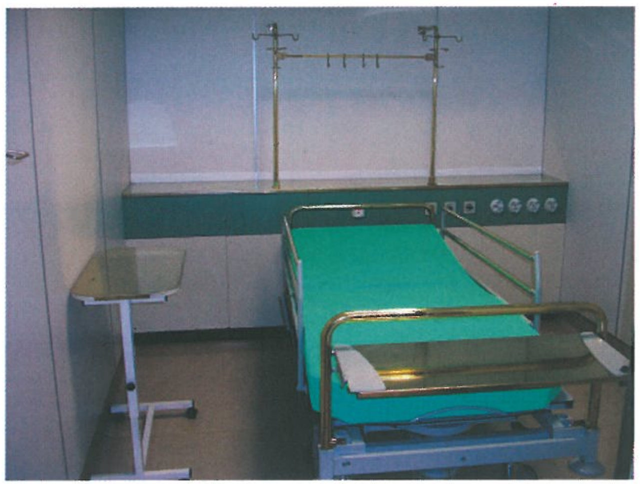

Figure 1: TOKUDA's hospital isolations units (Sofia, Bulgaria)

Antimicrobial activity of copper (Mechanism of Action)

In the conduct of copper we know that the copper atom emits ions and alter the valence from 0 to + and ++. Copper ions, in the basic research of Marc Solioz, upon contact with microbes, generates electric deregulation and disorder the pump of K - Na which is located in the cell membrane thereof. This action creates osmotic problems in the cell, thereby killing the microbes (3). It is important that the hydroxyls release during "Fenton phenomenon" (see formula*) creates the conditions for the continuous release of copper ions due to the conversion of monovalent or divalent and vice versa, resulting in further killing of microbes in the region. In such process, the action of copper ions released create disturbance in the action of DNA replication within the virus propagation period. Based on the above, the microbicidal and virucidal activity of the antimicrobial copper is completed in two hours time (Figure 2.) when the surface contacts microbes and viruses. These theories have been recorded by a group of scientists of the Universities of Bern and Nebraska and are still in progress

(3). In other theoretical models scientists try to explain the germicidal and virucidal of antimicrobial copper surfaces, the effect of copper ions studied in wet and dry environment with obvious superiority germicidal action on dry surfaces (7).

1. $H_2O_2 + O_2^{-} \rightarrow O_2 + OH^{-} + OH^{\cdot}$
2. $Cu\,(II) + O_2^{-} \rightarrow Cu\,(I) + O_2$
3. $Cu\,(I) + H_2O_2 \rightarrow Cu\,(II) + O_2 + OH^{-} + OH.$

- *Rate constant for Fe(II) Fenton reaction is 76 M-1.sec-1 (Walling, 1975)*
- *60x faster for Cu(I) 4700 M-1.sec-1 (Halliwell and Gutteridge, 1990)*

Figure 2. Fenton reaction

The Hellenic Copper Development Institute's (HCDI) Scientific Group has approached this issue by giving an interpretation to the phenomenon and introducing the theoretical view that the germ and virus activate the copper atom to the emission of ions with their acidic environment, which respectively kills - inactivates them.

The following Figure 3. describes the phases of antimicrobial copper actions.

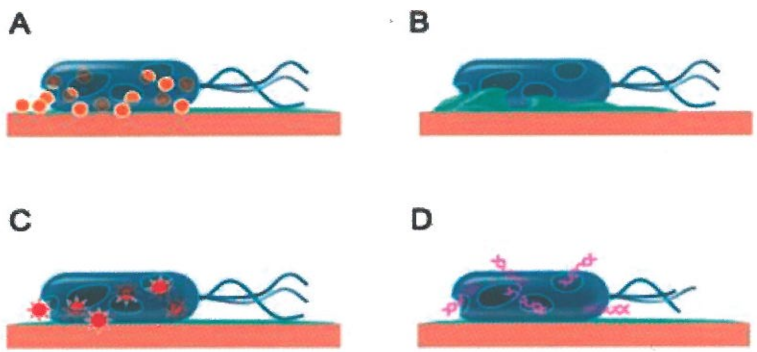

Figure 3: Antimicrobial copper microbiocidal activity

Completed Medical researches

Worldwide in the last decade and after the completion of the basic researches conducted in the US by Schmidt, Salgado et al (8) and in various scientific centers completed research flows on the direction of:

A. The application of antimicrobial copper in hospital environ ment and especially in Intensive Care Units (9)

B. The application of antimicrobial copper in public places such as schools, kindergartens, hotels, etc.

C. The application of antimicrobial copper in various utilitarian character objects such as medical earphones, medical thermometers, pens, PC keyboards etc and most recently

D. The application of antimicrobial copper for aquacultures.

Professor Keevil of Birmingham's University in the researches concerning the action of antimicrobial copper in noroviruses that are directly related to gastroenteritis, claims that surfaces with antimicrobial copper destroy noroviruses in a period of less than two hours so that the use of copper alloys objects to protect public health.

Professor Schmidt in his research indicates that the impact of reducing infections in hospitals where antimicrobial copper objects are placed, is significantly relative to materials such as wood, steel and plastic (8,10).

It is important that the main antimicrobial copper application recording, in the hospital environment, concerns mainly Salgado and colleagues' Intensive Care Units reporting that microbial strains such as MRCA and VRE were decreased significantly in intensive care units where antimicrobial copper alloys were used. (11) Emphasis was placed by Schmidt and his colleagues on the use of antimicrobial copper in ICU s' door handles which is the best choice for this innovative method. (12)

The reduction of nosocomial infections has been significantly affected after the use of these materials, resulting in the reduction of antibiotic use and the time of hospitalization. In the economic study of Gadi - Efstathiou the economic assimilation in 34% of costs at the use of antimicrobial copper in intensive care unit is being highlighted. (13)

In this study, in an intensive care unit (mixed type) the medical and economic data were recorded and analyzed in two different time periods; before and after the application of antimicrobial copper alloy Cu 63% - Zn 37% (Low Lead). This alloy was used for the manufacture and application of various objects and surfaces and was certified for its' antimicrobial actions by the Environmental Protection Agency (EPA) in the USA and the Hellenic Copper Development Institute (HCDI).

All doors, trolleys and cabinets' handles as well as nurse's station and trolleys' surfaces are of antimicrobial copper. Cultures were collected before and after the phase of copper plating in order to observe microbial growth and isolation of viruses with antibiograms for the determination of the antibiotics that are sensitive to them. Molecular techniques were used for viruses' isolation. Parameters such as patients' severity of disease classification system SAPS II (Simplified Acute Physiology Score) and APACHE II (Acute (Acute Physiology And Chronic Health Evaluation) in the intensive care unit were statistically analyzed with the statistical analysis software package SPSS 18. It is significant that in this study before and after the copper plating dose per day per patient (ddp) consumption of antimicrobial drugs were determined.

Researchers report that the reduction of infection in two different time periods was at a rate of 40.4%, and it is concluded that the reduction on antimicrobial drugs was statistical significant.

Also, studies which have been conducted by Noyce and his research team demonstrated the inactivation of influenza virus on antimicrobial copper surfaces above 90% after 6 hours when compared to corresponding surfaces of steel (14).

Regarding specific strains on which specialized researches were conducted, antimicrobial copper's action and inactivation of the germicide - hemolytic staphylococci (Staphylococcus Haemolyticus) by destroying the cell membrane were demonstrated by Santo et al. (15) In another scientific research M.Souli et al. demonstrate the primacy of anti microbial copper against clinically isolated Gram- bacteria such as K.pneumoniae, P.aeruginosa, Acinetobacter, Enterobacter spp. (16). In this study 24 clinically isolated Gram- bacteria (producing carbapenemase) were studied in 4 different surfaces. These surfaces were made of 99% pure copper and copper alloy (63%) in correspondence with polyvinyl chloride (PVC) and steel (stainless steel-SS).

The results showed that copper has statically significant microbicidal activity in multidrug-resistant nosocomial gram- pathogens. Also it is noted by researchers that it is important beyond the use of antimicrobial surfaces, to promote respected cleaning protocols and good hygiene practices in clinical settings in order to prevent nosocomial infections.

One of the most important healthcare applications was presented by Anagnostakou researchers and collaborators with the application of antimicrobial copper in a Neonatal Intensive Care Unit (NICU) of a pediatric hospital. In this case, the unit was implemented with copper alloy whose composition was of Cu63% - Zn37% (Low - Lead) and were culture samples were collected using two methods; wet and dry technique.

Survey results indicate a statistically significant reduction of microbial flora on surfaces and objects made of antimicrobial copper ($n = 21$, $p = 0{,}031 < 0{,}05$) at a rate of 95-100%. Pathogens isolated before copper plating were: Klebsiella spp., Staph. Epidermidis, staph. Aureus, Enterococcus spp. Significance of the study is focused on the reduction of microbial flora in this unit as well as in the neonatal intensive care unit where neonatal infections are the most common cause of morbidity and mortality in preterm infants.

Generally, there are researches which have investigated the effectiveness of copper ions' action on a large number of Gram + and Gram- microbes in touch surfaces of the above alloys. (17)

Antimicrobial Copper Implementations in the Community - Public Health

In the frame of antimicrobial copper implementation for microbial flora reduction, the scientific team of the Hellenic Copper Development Institute (HCDI) proceeded with the implementations in basic schools (primary) in the area of Athens. In cooperation with the educational community antimicrobial alloys were used in five elementary schools in the areas of Filothei and Ekali.

According to the researchers report (18) all staircases' railings and all doors' handles were replaced and covered with antimicrobial copper. Those touch points were estimated to be of high frequency usage by the students. The studies were conducted over a period of 3 years and recorded all microbiological loads at points of contact before and after the antimicrobial copper implementation.

Fig 4: Banister made of antimicrobial copper in the primary school unit

As the researchers report stratified study of epidemiological data before and after the use of antimicrobial copper, was made. The project is considered one of the world's largest antimicrobial copper implementation in educational institutions, since there have been similar projects in Japan in respective kindergartens (18).

The results showed a clear reduction of microbial flora in the replaced touch points (see. Figures) including epidemiological data reduction, especially for data related to seasonal flu. The use of antimicrobial copper in the community is observed in the last eight years also in other areas.

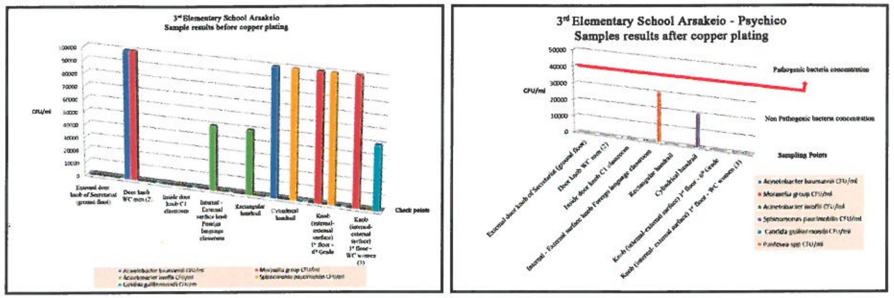

Fig 5: Reduction on primary school's microbial flora after antimicrobial copper installation

As stated in the CDA-UK a large number of hotels, metros', utility buildings, etc. have been using antimicrobial copper in the frame of public health protection.

In line with the above we mention the development of the first antimicrobial thermometer from a Greek medical industry the "Alfa check thermometer" (worldwide patent). Clinical studies for the thermometer (19) showed that the specific digital axillary thermometer 2 hours after its use was found microbe free on its entire surface (99% activity). It is significant as the researchers report that the effect of antimicrobial copper at the 2 ends (photo) affects the rest

Fig 6: Digital antimicrobial copper thermometer for auxillary use

of the device based on the 'HALO' phenomenon (phenomenon "Stefanis"). This phenomenon was first studied in this research. Other implementations as reported by the CDA-UK are the antimicrobial stethoscope, the antimicrobial computer keyboard and the antimicrobial pen.

Conclusions

It is known that healthcare associated infections (HCAI's) are currently the greatest risk against the protection of public health. The World Health Organization classifies these infections as "first risk" and rings the alarm for the rational use of antibiotics aiming to the non-development of resistant strains.

In line with the above, the European Center for Disease Prevention and Control (ECDC) indicates that millions of people are infected each year. Especially at the Intensive Care Units, 51% of patients develop nosocomial infections.

This is translated into longer days of hospitalization in the intensive care unit, increased risk for their lives and greater financial burden on the health system. At this point great emphasis is given by the World Health Organization and the European Center for Disease Prevention and Control (ECDC), to reduce microbe transfer from one surface to another. For the past 15 years, precautionary instructions have been issued in order to limit the transfer of microbes from the medical and nursing staff to the patients and vice versa.

The use of antimicrobial copper alloys over 60% has been proven worldwide as a mean of containment and reduction of microbial flora mainly in hospital environment and the results of the reduction of the microbial load are no other than consequent reduction of both nosocomial infections and the use of the respective antibiotics provided.

The above is a clear evident that will affect the economics of hospitals with multiple benefits for the economy of a state.

Under the current conditions of the worldwide economic crisis we experience at this period, innovative applications as antimicrobial copper enhance at a significant degree the operation and the effectiveness of public health.

It is important at this point to emphasize that the campaign of the World Health Organization " Clean Care is Safer Care " (clean hands) should be continued while the efforts to reduce the use of antibiotics to not create resistant strains should constitute the main core of medical effort in the fight against microbes.

In Greece there is a total number of 13 antimicrobial copper implementations in the public and private sector.

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